Practitioner's Docket No. **1540/144** ***PATENT***

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

re application of: Simpkins

Application No.: 10/082,812 Group No.: 1614
Filed: February 25, 2002 Examiner: Weddington, K.
For: Methods of Prevention of Treatment of Ischemic Damage

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
ATTENTION: GROUP DIRECTOR

TRANSMITTAL OF SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT AFTER MAILING DATE OF FINAL ACTION, NOTICE OF ALLOWANCE OR ACTION THAT CLOSES PROSECUTION BUT BEFORE PAYMENT OF ISSUE FEE (37 C.F.R. § 1.97(d))

CERTIFICATION UNDER 37 C.F.R. §§ 1.8(a) and 1.10*

*(When using Express Mail, the Express Mail label number is **mandatory**; Express Mail certification is optional.)*

I hereby certify that, on the date shown below, this correspondence is being:

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11/28/2003 AWONDAF1 00000050 10082812
02 FC:1806 180.00 OP

Signature

Date: November 21, 2003

BARBARA J. CARTER, PH.D.
(type or print name of person certifying)

** Only the date of filing (' 1.6) will be the date used in a patent term adjustment calculation, although the date on any certificate of mailing or transmission under ' 1.8 continues to be taken into account in determining timeliness. See ' 1.703(f). Consider "Express Mail Post Office to Addressee" (' 1.10) or facsimile transmission (' 1.6(d)) for the reply to be accorded the earliest possible filing date for patent term adjustment calculations.*

TIME OF TRANSMITTAL OF ACCOMPANYING SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

1. The information disclosure statement transmitted herewith is being filed ***after*** a final action under § 1.113, or a notice of allowance under § 1.311, whichever occurs first, but before, or simultaneously with, the payment of the issue fee.

STATEMENT AND FEE

2. In accordance with the requirements of 37 C.F.R. § 1.97(d):

   A. Accompanying this transmittal is a statement, as specified in 37 C.F.R. § 1.97(e).
   B. Applicant submits the fee set forth in § 1.17(p) ($180.00).

FEE DUE

3. Fee due (§ 1.17(p)): $180.00

METHOD OF PAYMENT OF FEE

4. Attached is a check in the amount of $180.00.

   A duplicate of this paper is attached.

Date: November 21, 2003

01540/00144 281735.1

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Practitioner's Docket No. **1540/144** ***PATENT***

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent application

_____

Inventor(s)

for _____

Title of invention

_____

the specification of which is being transmitted herewith

OR

In re application of: Simpkins

Application No.: 10/082,812 Group No.: 1614
Filed: February 25, 2002 Examiner: Weddington, K.
For: Methods of Prevention of Treatment of Ischemic Damage

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATION UNDER 37 C.F.R. SECTIONS 1.8(a) and 1.10*
*(When using Express Mail, the Express Mail label number is **mandatory**;*
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I hereby certify that, on the date shown below, this correspondence is being:

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37 C.F.R. SECTION 1.8(a) **37 C.F.R.SECTION 1.10***

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TRANSMISSION

☐transmitted by facsimile to the Patent and Trademark Office.

Signature Barbara J Carter

Date: November 21, 2003

Barbara J. Carter, Ph.D.
(type or print name of person certifying)

***WARNING:** *Each paper or fee filed by "Express Mail" **must** have the number of the "Express Mail" mailing label placed thereon prior to mailing. 37 C.F.R. section 1.10(b).*
*"Since the filing of correspondence under section 1.10 without the Express Mail mailing label thereon is an oversight that can be avoided by the exercise of reasonable C.F.R.e, requests for waiver of this requirement will **not** be granted on petition." Notice of Oct. 24, 1996, 60 Fed. Reg. 56,439, at 56,442.*

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

NOTE: "An information disclosure statement shall be considered by the Office if filed by the applicant:
(1) Within three months of the filing date of a national application;
(2) Within three months of the date of entry of the national stage as set forth in section 1.491 in an international application; or
(3) Before the mailing date of a first Office action on the merits, whichever event occurs last." 37 C.F.R. section 1.97(b).

NOTE: "Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability as defined in this section." 37 C.F.R. section 1.56(a).
"Individuals associated with the filing or prosecution of a patent application within the meaning of this section are:
(1) each inventor named in the application;
(2) each attorney or agent who prepares or prosecutes the application; and
(3) every other person who is substantively involved in the preparation or prosecution of the application and who is associated with the inventor, with the assignee or with anyone to whom there is an obligation to assign the application." 37 C.F.R. section 1.56(c).

NOTE: The "duty as described in section 1.56 will be met so long as the information in question was cited by the Office or submitted to the Office in the manner prescribed by sections 1.97(b) - (d) and 1.98 before issuance of the patent." Notice of January 9, 1992, 1135 O.G. 13-25 at 17.

***WARNING:** "No information disclosure statement may be filed in a provisional application." 37 C.F.R. section 1.51(b).*

List of Sections Forming Part of This Supplemental Information Disclosure Statement

The following sections are being submitted for this Information Disclosure Statement:

(check sections forming a part of this statement: disC.F.R.d unused sections and number pages consecutively)

1. [x]Preliminary Statements
2. [x]Forms PTO/SB/08A and 08B (substitute for Form PTO-1449)
3. [ ]Statement as to Information Not Found in Patents or Publications
4. [ ]Identification of Prior Application in Which Listed Information Was Already Cited and for Which No Copies Are Submitted or Need Be Submitted
5. [ ]Cumulative Patents or Publications
6. [x]Copies of Listed Information Items Accompanying This Statement
7. [x]Concise Explanation of Non-English Language Listed Information Items
   - 7A. [ ]EPO Search Report
   - 7B. [ ]English Language Version of EPO Search Report
8. [ ]Translation(s) of Non-English Language Documents
9. [ ]Concise Explanation of English Language Listed Information Items (Optional)
10. [x]Identification of Person(s) Making This Information Disclosure Statement

(complete the following, if appropriate)

Sections , respectively, have been continued on ADDED PAGE(S).

NOTE :"Once the minimum requirements are met, the examiner has an obligation to consider the information." Notice of April 20, 1992 (1138 O.G. 37-41, 37).

Section 1. Preliminary statements

Applicants submit herewith patents, publications or other information, of which they are aware that they believe may be material to the examination of this application, and in respect of which, there may be a duty to disclose.

The filing of this information disclosure statement shall not be construed as a representation that a search has been made (37 C.F.R. section 1.97(g)), an admission that the information cited is, or is considered to be, material to patentability, or that no other material information exists.

The filing of this information disclosure statement shall not be construed as an admission against interest in any manner. Notice of January 9, 1992, 1135 O.G. 13-25, at 25.

SECTION 2. FORMS PTO/SB/08A and 08B (formerly Form PTO-1449)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Simpkins	Attorney Docket:	1540/144
Serial No:	10/082,812	Art Group Unit:	1614
Date Filed:	February 25, 2002	Examiner Name:	Weddington, K.
Invention:	Methods of Prevention of Treatment of Ischemic Damage		

LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

U.S. PATENT DOCUMENTS					
Examiner Initials	**Reference Number**	**Document Number**	**Issue Date**	**Inventor**	**Class/Subclass**
	BB	US 5,512,557	04/30/1996	Collins, P.	514/182
	BC	US 6,319,914	11/20/2001	Simpkins, et al.	514/182
	BD	US 6,326,365	12/04/2001	Simpkins, et al.	514/179
	BE	US 6,339,078	01/15/2002	Simpkins, et al.	514/179

FOREIGN PATENT DOCUMENTS						
Examiner Initials	**Reference Number**	**Country Code**	**Document Number**	**Publication Date**	**Patenteee or Applicant**	**Class/Subclass**
	BF	**EP**	0 753 300 B1	06/27/1996	Oettel, et al.	A61K 31/565
	BG	**JP**	08165242	06/25/1996	Yagi Kunio	A61K 31/565
	BH	**WO**	94/28905	12/22/1994	Goddar, H.	A61K 31/565
	BI	**WO**	95/12402	05/11/1995	Simpkins, et al.	A61K 31/565
	BJ	**WO**	95/13076	05/18/1995	Droescher, P.	A61K 31/565

Examiner Signature: _____

Date Considered: _____

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation *if not* in conformance and not considered. Include copy of this form with next communication to applicant.

Section 6. Copies of Listed Information Items Accompanying This Statement

NOTE: 37 C.F.R. section 1.98(a)(2) requires that any information disclosure statement filed under section 1.97 shall include: "A legible copy of: (1) Each U.S. and foreign patent; (ii) Each publication or that portion which caused it to be listed; and (iii) All other information or that portion which caused it to be listed, except that no copy of a U.S. patent application need be included . . ."

NOTE: The wording in section 1.98(a)(2)(iii) makes it clear that the requirement to submit a copy of each item of information listed in an information disclosure statement does not apply to the citation of a U.S. patent application. Notice of January 9, 1992, 1135 O.G. 13-25, at 14.

Legible copies of all items listed in Forms PTO/SB/08A and 08B (substitute for Form PTO-1449) accompany this information statement.

(complete the following, if applicable)

[ ]Exception(s) to above:

[ ]Items in prior application, from which an earlier filing date is claimed for this application, as identified in Section 4.

[ ]Cumulative patents or publications identified in Section 5.

Section 7. Concise Explanation of Non-English Language List Information Items

NOTE: *"A concise explanation of the relevance, as it is presently understood by the individual designated in section 1.56(c) most knowledgeable about the content of the information of each patent, publication, or other information listed that is not in the English language shall be included in any information disclosure statement filed under section 1.97. The concise explanation may be either separate from the specification or incorporated therein." 37 C.F.R. section 1.98(a)(3).*

NOTE: *"[T]he explanation required is limited to the relevance as understood by the individual designated in section 1.56(c) most knowledgeable about the content of the information at the time the information is submitted to the Office." Notice of January 9, 1992, 1135 O.G. 13-25 at 14.*

NOTE: *"Where the information listed is not in the English language, but was cited in a search report by a foreign patent officer, the requirement for a concise explanation of relevance is satisfied by submitting an English language version of the search report." Notice of January 9, 1992, 1135 O.G. 13-25. at 14.*

NOTE: *"The concise explanation requirement for non-English language information may be met by submission of an English language version of the search report indicating the degree of relevance found by the foreign office." Notice of January 9, 1992, 1135 O.G. 13-25, at 20.*

WARNING: *"The requirement in section 1.98(a)(3) for a concise explanation of non-English language information would not be satisfied by a statement that a reference was cited in the prosecution of a parent application." Notice of January 9,1992, 1135 O.G. 13-25 at 20 (emphasis added).*

Section 10. Identification of Person(s) Making This Information Disclosure Statement

The person making this certification is

(check each applicable item)

(a) [ ]the inventor(s) who signs below

_____

SIGNATURE OF INVENTOR

_____

(type name of inventor who is signing)

(b) [ ]an individual associated with the filing and prosecution of this application (37 C.F.R. section 1.56(c))

_____

SIGNATURE OF INVENTOR

_____

(type name of inventor who is signing)

(c) [x] the practitioner who signs below on the basis of the information:

(check each applicable item)

[ ] supplied by the inventor(s).

[ ] supplied by an individual associated with the filing and prosecution of this application. (37 C.F.R. section 1.56(c)).

[x] in the practitioner's file.

Barbara J. Carter

SIGNATURE OF PRACTITIONER

Reg. No.: 52,703

Barbara J. Carter, Ph.D.

(type or print name of practitioner)

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125 Summer Street, 11th Floor

P.O. Address

Customer No.: 002101

Boston, MA 02110

01540/00144 281708.1

Concise Explanation of Non-English Language Documents Listed in the Supplemental Information Disclosure Statement Filed November 21, 2003

- Reference EP 0 753 300, discloses the use of 17α estradiol in older males over a 6-month period, whose blood was evaluated for cholesterol and other components. Pp. 8-9. There is no disclosure or suggestion of mitigating the effects of a future ischemic event by administration of a prophylactic amount of a non-sex hormone.

  Claim 1 reads: Use of 17α-estradiol, the chemically modified derivatives thereof or the esters of 17α-estradiol or the chemically modified derivatives thereof having antioxidant properties, with the exception of ethynylestradiol, for the production of pharmaceutical preparations for the prevention and treatment of chronic-degenerative diseases of the brain, of atherosclerosis and arthritis/osteoarthritis in humans.

- Reference WO 94/28905, discloses the use of estriol or compositions that release estriol (for example, p.3, last par.) for prophylactic and therapeutic purposes in connection with atherosclerosis (pp. 6-7). There is no disclosure or suggestion of mitigating a future ischemic event by administration of a prophylactic amount of a non-sex hormone.

- Reference D5, WO 95/13076, discloses, on the basis of *in vitro* analysis, use of compositions having phenolic A-ring structures (excluding estradiol, estrone, estrione and various derivatives) for prophylactic and therapeutic purposes in connection with cells suffering damage from exposure to free radicals. The only experiments recited (p. 3, line 20 to p. 7, line 17, and pp. 9-11) are *in vitro* (p. 7, line 9), aimed at evaluating the effect of various radical-scavenging substances in inhibiting lipid peroxidation and LDL oxidation. On the basis only of this experimental data, the reference speculates that the compositions have applicability "for prophylaxis and therapy, to cell damage caused by radicals, in the case of spinal trauma, ischemic (thromboembolismic) stroke, ischemia, organ damage in the reperfusion phase after transplantation, chronic degenerative diseases of the CNS, senile dementia of the Alzheimer type, asthma, muscular dystrophy and degenerative neurological illness, and other forms of CNS intoxication or degeneration conditions" (p. 7, lines 19-28). No dosage or administration regime is offered, so the reference is not enabling in respect to these speculative uses. Moreover, there is no disclosure of mitigating a future ischemic event by administration of a prophylactic amount of a non-sex hormone.

- Reference D6, Patent Abstracts of Japan, publication number 08166241, discloses use of an estrogen *metabolite* for use as an anti-arteriosclerotic agent that is capable of suppressing the hyperplasia of the arterial smooth muscle cells. There is no disclosure or suggestion of mitigating a future ischemic event by administration of a prophylactic amount of a non-sex hormone.